DETAILED ACTION

A request for continued examination under 37 C.F.R. 1.114, including the fee set forth in 37 C.F.R. 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 C.F.R. 1.114, and the fee set forth in 37 C.F.R. 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 C.F.R. 1.114. Applicant's submission filed February 18, 2011 has been received and entered into the present application. Claims 1-13 are under examination in the instant office action.

Applicants' arguments and declaration under 37 CFR 1.132, filed on February 18, 2011, have been fully considered but they are moot in view of a new ground of rejection. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1,148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35

U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.

3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-13 are rejected under 35 U.S.C. § 103(a) as being unpatentable over WO 2004/105751 (Barone *et al.*, prior art of record) in view of Campese (Hypertension, 23(4): 531-550, 1994), 1994), Dustan *et al.* (Am J Med Sci., 292(2):67-74, 1986, abstract) and Tanahashi *et al.* (J Pharma Exp Thera, 289:1533-1538, 1999).

Barone *et al.* teaches a method of reducing cardiovascular pathology such as cardiac hypertrophy, heart failure, congestive heart failure, and sodium and water retention in a mammal suffering from hypertension, comprising administering an effective amount of PDE4 inhibitor, wherein the PDE4 is a PDE4 specific inhibitor such as rolipram (RS)-4-(3-cyclopentyloxy-4-methoxy-phenyl)pyrrolidin-2-one) (p10, lines 23-30, p3, lines 16-31, claims 1, 5, and 7-8). The PDE4 inhibitor, rolipram is the elected species, thus it meets limitations recited in claims 2-10 since Applicant stated that claims 1-13 reads on rolipram in the response filed on 8/13/2009. It further teaches the use of PDE4 inhibitor includes veterinary use as well as human use (p10, lines 9-13 and p4, lines 22-24).

The reference differs from the instant claims insofar as it does not specifically teach that the hypertension is a salt-sensitive hypertension.

Campese teaches that 51% of patients with hypertension are classified as salt-sensitive, 16% as salt resistant, and the remaining as having an intermediate response (p532, col 1, para 1). Campese also teach that salt-sensitive patients are more likely than salt-resistant patients to manifest left ventricular hypertrophy, microalbuminuria and metabolic abnormalities that may predispose them to cardiovascular disease and salt sensitivity in hypertension is associated with substantial renal, hemodynamic, and metabolic abnormalities that may enhance the risk of cardiovascular and renal morbidity (abstract). In addition, Campese teaches that one frequent finding among salt sensitive patients with essential hypertension is an increase in sodium retention during NaCl diet (p532, col 1, last paragraph).

Dustan *et al.* teach that excessive sodium retention as a characteristic of salt-sensitive hypertension (abstract).

Tanahashi *et al.* teaches that the inhibition of PDE IV with a specific PDEIV inhibitor such as rolipram enhances glomerular filtration and urinary Na^+ secretion with elevating arterial and renal venous plasma cAMP concentrations and urinary cAMP excretion (abstract, Table 3, figures 2 and 4).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the PDE4 inhibitor such as rolipram taught by Barone *et al.* for the treatment of salt-sensitive hypertension as suggested and motivated by the combined teachings of the cited references. As stated above, the selective PDE4 inhibitors such as rolipram are taught to be useful for reducing cardiovascular pathologies such as cardiac hypertrophy, heart failure, congestive heart failure, and sodium and water retention in a mammal suffering from hypertension by Barone *et al.* and are also known to be effective for enhancing glomerular

filtration and urinary Na^+ secretion as evidenced by Tanahashi *et al.* Campese teaches that more than 51% of patients with hypertension are classified as salt-sensitive and that salt-sensitive patients are more likely than salt-resistant patients to manifest cardiovascular pathologies such as left ventricular hypertrophy, microalbuminuria and metabolic abnormalities and redispose them to cardiovascular disease. In addition, Campese and Dustan *et al.* teach that excessive sodium retention as a characteristic of salt-sensitive hypertension. Therefore, the skilled artisan would have been motivated to use the PDE4 inhibitor such as rolipram in the treatment of salt-sensitive hypertension on the reasonable expectation that it would reduce cardiovascular pathologies such as cardiac hypertrophy, heart failure, congestive heart failure, and sodium retention in a mammal suffering from salt-sensitive hypertension as taught by Barone *et al.* and Tanahashi *et al.*

From the teachings of the references in combination, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Claim Objections

Claims 6-9 are objected to under 37 CFR 1.75 as being a substantial duplicate of claims 2-5, respectively. When two or more claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BONG-SOOK BAEK whose telephone number is 571-270-5863. The examiner can normally be reached 9:00 am-6:00 pm Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Lundgren can be reached on 571-272-5541. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/BONG-SOOK BAEK/

Examiner, Art Unit 1629